UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,889	12/15/2003	Elias Georges	112418-147 and AUR-013US	5738

23483 7590 05/03/2006

WILMER CUTLER PICKERING HALE AND DORR LLP
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/736,889	GEORGES ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-108* is/are pending in the application.

4a) Of the above claim(s) *11,13,20-58,67,69 and 75-108* is/are withdrawn from consideration.

5)☒ Claim(s) *1-9 and 59-65* is/are allowed.

6)☒ Claim(s) *10,12,14-19,66,68 and 70-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed on 3/1/06 in response to the previous Non-Final Office Action (9/21/05) is acknowledged and has been entered.

Claims 11, 13, 20-58, 67, 69, 75-108 have been withdrawn for non-elected invention.

Claims 1-108 are pending. Claims 1-10, 12, 14-19, 59-66, 68, 70-74 are under consideration.

The text of those sections of Title 35, U.S.Code not included in this action can be found in the prior Office Action.

The following office action contains NEW GROUNDS of rejection.

Information Disclosure Statement

The information disclosure statement (s) (IDS) submitted on 3/22/06 are/is considered by the examiner and initialed copy of the PTO-1449 is enclosed.

Rejections Withdrawn

All rejections from prior Office action are withdrawn in view of Applicant arguments and in light of changing the prior art in the rejection.

The following is a New Ground of rejection

Specification

Specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 73, line 25, page 99, line14, and page 100, line 29. Applicant is required to check entire specification and delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Rejection under 35 U.S.C. 103(a)

1. Claims 10, 12 and 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meschini et al., (Int, J. Cancer, Vol 87, page 615-628, 2000) in view of Fanger et al., (US Patent NO: 5762930, 1998) and Heidenthal et al., (Biochem Biophys Res Comm, vol 267, page 49-53).

The claims as written just require that LDL bind to cell surface vimentin. There is no exclusion of cytoplasmic vimentin. While Applicants does state "specifically". "Specifically" has not been defined in the specification as only limited to cell surface expressed vimentin. Applicant is cautioned against the addition of new matter.

Meschini et al., teach a method of measuring the expression of vimentin in Multidrug Resistant (MDR) neoplastic cells. Meschini et al., first teach that drug resistant cells express MDR protein, p-glycoprotein, (page 620, page 4 and page 621, figure 5). Meschini et al., then, teach that the resistant cells display a high level of vimentin by flow cytometry analysis and immunocytochemical staining, which are correlated with MDR protein expression, while the drug sensitive cells express very low levels of vimentin (page 618, col 1, table II and page 619, figure 2). Meschini et al., further teach the expression of vimentin is determined by antibody to vimentin and measured by immunofluorescence emission (page 618, Table II and 619, figure 2). Although Meschini et al., do not specifically teach that expression of vimentin is on the cell surface of MDR neoplastic cells, figure 2 of the immunocytochemical staining of vimentin does suggest the surface expression of vimentin on the MDR cells.

Meschini et al., do not teach detecting MDR cells by modified LDL, a vimentin binding agent, linked to a detectable agent and detecting MDR by administering the vimentin binding agent.

Fanger et al., teach that administering LDL or AcLDL (modified LDL) to a patient, (column 3, para 1). Fanger et al., also teach the LDL is fluorophores-labeled or radiolabeled, which bind to the cell expressing LDL binding protein on the surface in vivo (column 3 para 2 and column 11, para 1).

Heidenthal et al., teach that modified LDL binds to vimentin (entire article).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to detect the MDR cells in a patient by measuring the level of modified LDL administered and bound to the vimentin expressed on the surface of the MDR cells in a patient. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Fanger et al., and Heidenthal et al., to Meschini et al., to detect the MDR cells by detecting the levels of labeled modified LDL binding on the surface of the MDR cells in a patient because Meschini et al., has suggested that a high level of vimentin comprising surface expressed vimentin is

detected in the MDR cells compared to the drug sensitive cells, Fanger et al., has shown that administered labeled LDL binds to the cells expressing LDL binding protein and Heidenthal et al., has shown modified LDL binds to vimentin. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to replace the antibody to vimentin taught by Meschini et al., with the modified LDL taught by Heidenthal et al., and determine MDR cells by measuring the levels of the modified LDL on the cell surface.

Applicants argue (page 13) that Heidenthal et al., reference does not teach that vimentin can be located on the surface of tumor cells, nor that cells surface-expressed vimentin is prognostic of MDR. In response to this argument, as discussed above, the primary reference by Meschini et al., does teach that vimentin is expressed on MDR tumor cells and also suggest vimentin is located on the surface of the tumor cells detected by vimentin binding agent, an antibody to vimentin. Heidenthal et al., teach another vimentin binding agent, modified LDL. Thus, in combination of teachings of Meschini et al., and Heidenthal et al., the references do suggest modified-LDL binds to vimentin, which is expressed on MDR tumor cells. It would be prima facie obvious to one of ordinary skill in the art to use the two teachings together to detect surface expressed vimentin by modified-LDL.

Applicants also argue (page 13) that Fanger et al., reference is limited to the administration of labeled LDL to patients and does not teach or suggest use of Labled LDL to detect cell surface expressed vimentin tumor cells or that cells surface-expressed vimentin is prognostic of MDR. In response to this argument, again as discussed above, the primary reference by Meschini et al., does teach that vimentin is expressed on MDR tumor cells and also suggest vimentin is located on the surface of the tumor cells. Fanger et al., teach administrating a patient labeled modified LDL, which could bind to the cell expressing LDL binding protein on the surface in vivo and Heidenthal et al., teach modified LDL is vimentin binding agent. Thus, in combination of teachings of Meschini et al., Fangerl et al., and Heidenthal et al., One of ordinary skill in the art would have been motivated with a reasonable expectation of success to detect in MDR tumor cells by administrating a patient labeled modified LDL, which bind to vimentin on the cell surface.

2. Claims 66, 68 and 70-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomas et al., (Clinical Cancer Research, Vol 5, page 2698-2703) in view of Fanger et al., (US Patent NO: 5762930, 1998) and Heidenthal et al., (Biochem Biophy res Comm (vol 267, page 49-53).

The claims as written just require that LDL bind to cell surface vimentin. There is no exclusion of cytoplasmic vimentin. While Applicants does state "specifically". "Specifically" has not been defined in the specification as only limited to cell surface expressed vimentin. Applicant is cautioned against the addition of new matter.

Thomas et al., teach the vimentin expression in the cells of breast cancer samples from breast cancer patients (page 2701, column 1, para 1). Thomas et al., teach a method of detecting vimentin expression determined by antibody for vimentin labeled with fluorescence dye (Rhodamine, figure 3, page 2701). Thomas et al., also teach that the method can be used for diagnosis of breast pathology and poor prognosis (page 2699, column 1, line 12-13). Although Thomas et al., do not specifically teach that expression of vimentin is on the cell surface of neoplastic cells, the figure 1 and 3, histological staining of vimentin on the breast cancer tissues do suggest that the expression of vimentin comprises the surface expression of the protein on the cells.

Fanger et al., teach that administering LDL or AcLDL (modified LDL) to a patient, (column 3, para 1). Fanger et al., also teach the LDL is fluorophores-labeled or radiolabeled, which bind to the cell expressing LDL binding protein on the surface in vivo (column 3 para 2 and column 11, para 1).

Heidenthal et al., teach that modified LDL binds to vimentin (entire article).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to detect neoplastic cells in a patient by measuring detectable levels of the modified LDL administered to a patient and bound to vimentin expressed on the neoplastic cells from the patient. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to combine the teachings of Fanger et al., and Heidenthal et al., to teaching of Thomas et al., to detect the neoplastic cell by detecting the modified LDL bound to the surface expressed vimentin on the cells because Thomas et al., have shown that vimentin is expressed in the neoplastic cell and the figures disclosed by the reference has suggested the expression of vimentin is detected on the surface of the

cells, and because Fanger et al., have shown that administered labeled LDL binds to the cells expressing LDL binding protein and Heidenthal et al., has shown that binding of modified LDL to vimentin.

Applicants arguments about the teachings by Heidenthal et al., and Fanger et al.,have been discussed above.

Conclusion

Claims 1-9 and 59-65 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

SHEELA HUFF
PRIMARY EXAMINER